



MR # 50780
8EHQ-0801-14996

INTERNATIONAL ISOCYANATE INSTITUTE, INC.

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August 13, 2001

TSCA Document Processing Center (TS-790)
Office of Toxic Substances
U.S. Environmental Protection Agency
401 M. Street, SW
Washington, DC 20460

ATTN: 8(e) Coordinator

RE: benzene, 1,1'-methylenebis[isocyanato-
CAS RN 26447-40-5

benzene, diisocyanatomethyl-
CAS RN 1321-38-6

Contain NO CBI

Dear Sir/Madam:

The following information is being submitted by the International Isocyanate Institute (III) on behalf of its members pursuant to current guidance issued by EPA indicating EPA's interpretation of Section 8(e) of the Toxic Substances Control Act. Neither III nor any member of III has made a determination as to whether a significant risk of injury to health or the environment is actually presented by the findings.

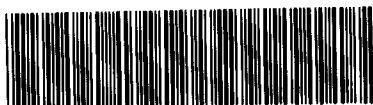
We are submitting an abstract by P. Romeo et al. that is to be presented at the European Respiratory Society in September of 2001. A decrease in Forced Expiratory Volume (FEV1) was reported in response to Specific Inhalation Challenge of persons sensitized to MDI or TDI. Two persons responded to the MDI challenge, one person responded to the TDI challenge. It was previously known that persons who are allergic to MDI or TDI might specifically react to low concentrations of these materials. The Romeo et al. study utilized a characterized exposure atmosphere. The change in FEV1 was modestly different than that observed in controls, though the authors considered this to be exposure-related.

Sincerely,

Jerry L. Fosnaugh
Managing Director

cjn

Enclosures



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**Abstract submitted for the European Respiratory Society meeting.
Berlin, Germany, September 2001**

Induced sputum profile after challenges to low concentrations (one ppb) of isocyanates.
P. Romeo, C. Lemière, J.-L. Malo. Department of Chest Medicine, Hôpital du Sacré-Coeur, Montréal, Canada.

Background and aim: There are anecdotal reports on the onset of asthmatic reactions after exposure to apparently very low concentrations of isocyanates. The recommended threshold concentration is < 5 ppb. We wanted to know if exposure to concentrations of isocyanates as low as one ppb can induce evidence of airway inflammation with or without functional changes. **Methods:** Six subjects with occupational asthma to isocyanates as previously demonstrated by specific inhalation challenges using isocyanates concentrations from 5 to 15 ppb underwent specific inhalation challenges with concentration of one ppb generated by a closed-circuit instrument (Cloutier Y. et al, 1992). FEV1 was assessed serially before and after challenges. Bronchial responsiveness to methacholine and induced sputum were assessed at the end of a control day and of a day of exposure to one ppb. **Results:** Three of the six exposed subjects had a late asthmatic reaction (falls in FEV1 of 20, 23 and 29% respectively) after exposure to concentrations of one ppb of isocyanates. Two of the three subjects showed a significant increase in the number of total cells and/or the % of neutrophils and the third had a significant increase in the % of eosinophils. A fourth subject had changes in FEV1 of 11% while showing a significant increase in the % of neutrophils. **Conclusion:** This study shows that: 1) subjects with occupational asthma to isocyanates can react to concentrations as low as one ppb; 2) neutrophils seem to be involved in the physiopathology of isocyanate-induced asthma. Supported by the International Isocyanate Institute.

Table 1. Inhalation challenges results

Subj.	Control day					Day of exposure to 1 ppb					
	PC20 (mg/ml)	Δ FEV1 (%)	Total cells(10^6)	Neutros (%)	Eos (%)	type of iso- cyanate	PC20 (mg/ml)	Δ FEV1 (%)	Total cells(10^6)	Neutros (%)	Eos (%)
no.1	1.4	-9.9	3.8	73	0.8	MDI	ND*	-28.5	114.1	98	0.5
no. 2	diluant	-2.4	1.9	23	22	HDI	0.06	-10.9	1.1	68	4
no.3	4.4	-3.3	1.4	22	0.2	MDI	ND*	-20.0	5.5	60	0
no.4	1.2	-2.6	2.5	55	1.5	TDI	ND*	-23.0	4.2	67	16
no.5	0.3	-9.8	0.95	49.5	1.2	TDI	0.2	-6.6	1.05	32	0.2
no.6	0.7	-9.2	22.2	81	2.3	HDI	0.7	0	20.5	78	2.5
no.7	0.03	0	1.80	50	7.8	HDI	0.07	-1.8	0.54	46	6.3

Day of positive reaction **

No.2	0.12	-21.9	1.23	57	5
No.5	ND	-33.8	1.29	54	2.5
No.6	0.8	-20.0	14	81	5.5
No.7	ND	-22.9	15.9	52	35

Legend: * the metacholine test was not performed because baseline FEV1 was lower than on the control day due to a late asthmatic reaction; ** include only those subjects (nos. 2, 5, 6 and 7) with a non-significant change in FEV1 on the day of exposure to 1 ppb.